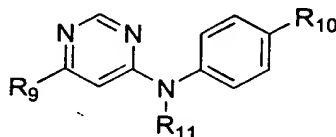


What is claimed is:

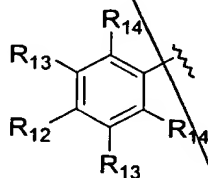
1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound having the formula



or a pharmaceutically acceptable salt thereof, wherein

- (a)  $R_9$  is selected from the group consisting of H, thienyl, furanyl, pyrrolyl, phenyl, substituted phenyl, pyridinyl, substituted pyridinyl, naphthyl, benzo[b]thien-2-yl, 2-benzofuranyl, pyrimidine and 2,4-(bismethoxyphenyl)-5-pyrimidinyl,

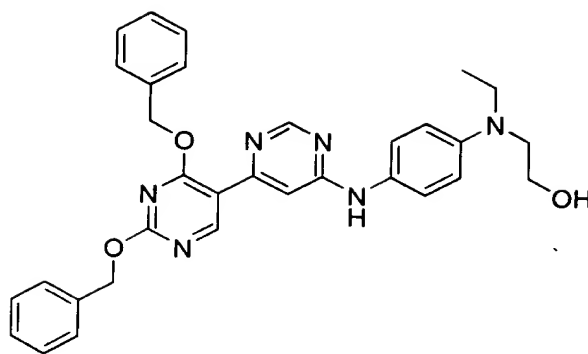
said substituted phenyl having the formula



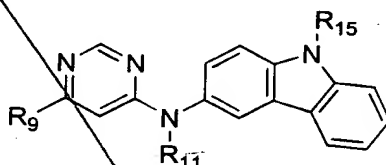
wherein (i)  $R_{12}$  is H, OH, lower alkylthio, alkoxy, alkylamine, dialkylamine, halogen-substituted lower alkyl, halogen substituted lower alkoxy, cyano, cyanoalkyl, phenyl, phenylalkoxy or substituted piperazinyl, N-(t-butoxy)carbamylalkyl, (ii) each  $R_{13}$  is independently H,  $NO_2$ , alkoxy, alkylamino, dialkylamino, halogen-substituted lower alkyl, halogen-substituted lower alkoxy or phenyl, and (iii) each  $R_{14}$  is independently H, alkoxy, phenyloxy or phenylalkoxy;

- (b)  $R_{10}$  is selected from the group consisting of cyanoalkyl, alkylamino, dialkylamino, hydroxy-substituted alkylamino and hydroxy-substituted dialkylamino; and
- (c)  $R_{11}$  is H or lower alkyl.

- 5c h
- 09922874-030601
2. The pharmaceutical composition of claim 1, wherein R<sub>9</sub> is substituted phenyl.
  3. The pharmaceutical composition of claim 1, wherein R<sub>11</sub> is H and R<sub>10</sub> is dialkylamino or hydroxy-substituted dialkylamino.
  - 5 4. The pharmaceutical composition of claim 1, wherein the compound is N1,N1-dimethyl-N4-[6-[4-(phenylmethoxy)phenyl]-4-pyrimidinyl]-1,4-benzenediamine.
  - 10 5. The pharmaceutical composition of claim 1, wherein the compound is N1-(6-[1,1'-biphenyl]-3-yl-4-pyrimidinyl)-N4,N4-dimethyl-1,4-benzenediamine.
  6. The pharmaceutical composition of claim 1, wherein the compound is N1-[6-[3,5-bis(trifluoromethyl)phenyl]-4-pyrimidinyl]-N4,N4-dimethyl-1,4-benzenediamine.
  - 15 7. The pharmaceutical composition of claim 1, wherein the compound is 2-[[4-[(6-[1,1'-biphenyl]-3-yl-4-pyrimidinyl)amino]phenyl]ethylamino]-ethanol.
  - 20 8. The pharmaceutical composition of claim 1, wherein the compound is 2-[[4-[(6-benzo[b]thien-2-yl-4-pyrimidinyl)amino]phenyl]ethylamino]-ethanol.
  9. The pharmaceutical composition of claim 1, wherein the compound is 2-[ethyl[4-[[6-[4-(trifluoromethoxy)phenyl]-4-pyrimidinyl]amino]phenyl] amino]-ethanol.
  - 25 10. The pharmaceutical composition of claim 1, wherein the compound is of the formula



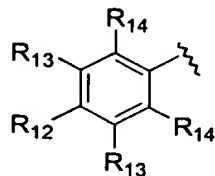
11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound having the formula



or a pharmaceutically acceptable salt thereof, wherein

- (a)  $R_9$  is selected from the group consisting of H, thienyl, furanyl, pyrrolyl, phenyl, substituted phenyl, pyridinyl, substituted pyridinyl, naphthyl, benzo[b]thien-2-yl, 2-benzofuranyl, pyrimidine and 2,4-(bismethoxyphenyl)-5-pyrimidinyl,

said substituted phenyl having the formula



wherein (i)  $R_{12}$  is H, OH, lower alkylthio, alkoxy, alkylamine, dialkylamine, halogen-substituted lower alkyl, halogen substituted lower alkoxy, cyano, cyanoalkyl, phenyl, phenylalkoxy or substituted piperazinyl, N-(t-butoxy)carbonylalkyl, (ii) each  $R_{13}$  is independently H,  $\text{NO}_2$ , alkoxy, alkylamino, dialkylamino, halogen-substituted lower alkyl,

halogen-substituted lower alkoxy or phenyl, and (iii) each  $R_{14}$  is independently H, alkoxy, phenyloxy or phenylalkoxy;

- (b)  $R_{11}$  is H or lower alkyl; and  
(c)  $R_{15}$  is H or alkyl.

5

Sub 12. A method for reducing ischemic death in a cell population comprising contacting the cell with a prophylactically effective amount of the compound of claim 1.

10 13. A method for reducing ischemic death in a cell population comprising contacting the cell with a prophylactically effective amount of the compound contained in the pharmaceutical composition of claim 11.

Sub 15 14. The method of claim 12, wherein the cell population comprises a cell selected from the group consisting of a neuronal cell, a glial cell, a cardiac cell, a lymphocyte, a macrophage and a fibroblast.

20 15. The method of claim 13, wherein the cell is selected from the group consisting of a neuronal cell, a glial cell, a cardiac cell, a lymphocyte, a macrophage and a fibroblast.

Sub 25 16. A method of reducing death in a cell population comprising neuronal cells in response to a traumatic event comprising contacting the neuronal cells with a prophylactically effective amount of the compound contained in the pharmaceutical composition of claim 1 prior to, during, or within a suitable time period following the traumatic event.

30 17. A method of reducing death in a cell population comprising neuronal cells in response to a traumatic event comprising contacting the neuronal cell with a prophylactically effective amount of the compound contained in the pharmaceutical composition of claim 11 prior to, during, or within a suitable time period following the traumatic event.

18. The method of claim 12 wherein the contacting is performed *in vitro*.

19. The method of claim 14, wherein the contacting is performed *in vitro*.

5 20. The method of claim 12, wherein the contacting is performed *ex vivo*.

21. The method of claim 14, wherein the contacting is performed *ex vivo*.

22. The method of claim 12, wherein the contacting is performed *in vivo*.

10 23. The method of claim 14, wherein the contacting is performed *in vivo*.

24. A method of reducing neuronal cell death in response to a traumatic event in a subject, comprising administering to the subject a prophylactically effective amount of the pharmaceutical composition of claim 1 prior to, during, or following the traumatic event.

15

20

25. A method of reducing neuronal cell death in response to a traumatic event in a subject comprising administering to the subject a prophylactically effective amount of the pharmaceutical composition of claim 11 prior to, during, or following the traumatic event.

26. The method of claim 24, wherein the subject is a human.

25 27. The method of claim 24, wherein the traumatic event is selected from the group consisting of a medical disorder, a physical trauma, a chemical trauma and a biological trauma.

28. The method of claim 24, wherein the pharmaceutical composition is administered prior to the traumatic event.

30

29. The method of claim 24, wherein the pharmaceutical composition is administered during the traumatic event.

Sub  
30. The method of claim 24, wherein the pharmaceutical composition is administered subsequent to the traumatic event.

5 31. The method of claim 25, wherein the subject is a human.

32. The method of claim 25, wherein the traumatic event is selected from the group consisting of a medical disorder, a physical trauma, a chemical trauma and a biological trauma.

10

33. The method of claim 25, wherein the pharmaceutical composition is administered prior to the traumatic event.

15

34. The method of claim 25, wherein the pharmaceutical composition is administered during the traumatic event.

35. The method of claim 25, wherein the pharmaceutical composition is administered subsequent to the traumatic event.

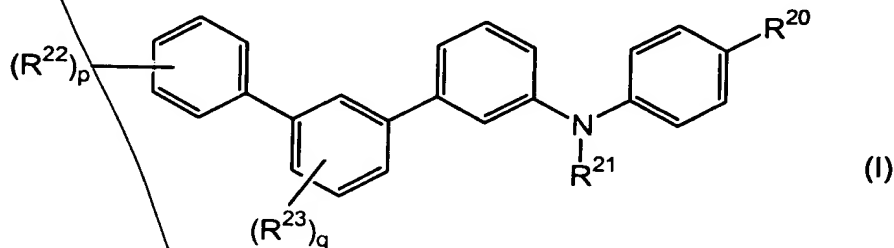
20 36. An apparatus for administering to a subject the pharmaceutical composition of claim 1 comprising a container and the pharmaceutical composition therein, wherein the container has a device for delivering to the subject a prophylactic dose of the pharmaceutical composition.

25 37. An apparatus for administering to a subject the pharmaceutical composition of claim 11 comprising a container and the pharmaceutical composition therein, wherein the container has a device for delivering to the subject a prophylactic dose of the pharmaceutical composition.

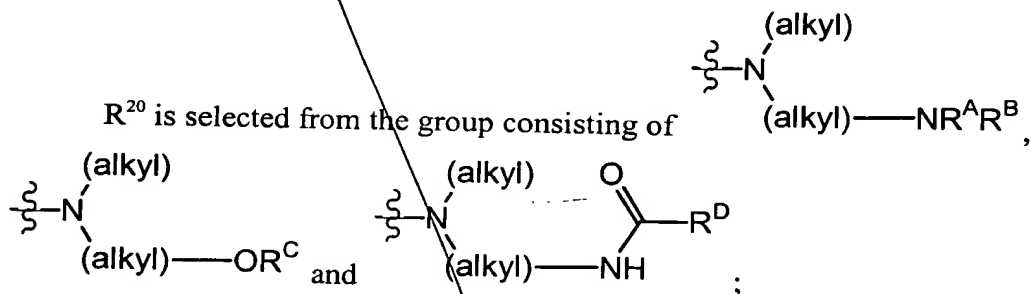
30 38. The apparatus of claim 36, wherein the device for delivering the pharmaceutical composition is a syringe.

39. The apparatus of claim 37, wherein the device for delivering the pharmaceutical composition is a syringe.

40. A compound of the formula



wherein



- wherein  $R^A$  and  $R^B$  are independently selected from hydrogen, alkyl, halogenated alkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, aralkyl, cycloalkyl, cycloalkyl-alkyl, heteroaryl, heteroaryl-alkyl, alkoxyalkyl, aryloxy, aryloxyalkyl, alkoxycarbonylalkyl and dehydroabietyl; wherein the aryl cycloalkyl, heteroaryl or heterocycloalkyl portion of any of the groups is optionally substituted with one or more substituents independently selected from
- halogen, alkyl, alkoxy, halogenated alkyl, amino, alkylamino, dialkylamino, arylamino, aralkylamino, amido, alkylamido, dialkylamido, arylamido, aralkylamido, azo, nitro, cyano, aryl, aralkyl, aryloxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, alkylthio, arylthio, alkylsulfonylN(H), or alkylsulfonylN(alkyl);

- alternatively  $R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form a compound selected from the group heteroaryl and heterocycloalkyl; wherein the heteroaryl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from halogen, alkyl, alkoxy, alkoxycarbonyl, halogenated alkyl, alkylcarbonyl, amino, alkylamino, dialkylamino, arylamino, azo, nitro or cyano;

Sub  
A<sup>3</sup>  
R<sup>a</sup> is selected from the group consisting of alkyl, aralkyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, (±)-N-benzoyl-aminoalkylcarbonyl or [3aS-(3α,4β,6α)]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-alkylcarbonyl;

5 R<sup>D</sup> is selected from alkyl, aryl, aralkyl, (±)-N-benzoyl-aminoalkyl, [3aS-(3α,4β,6α)]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-alkyl or biphenyl; wherein the alkyl or aryl portion of the alkyl, aryl or aralkyl group is optionally substituted with one or more substituents independently selected from halogen, alkyl, alkoxy, amino, alkylamino, dialkylamino, azo, nitro, cyano, or trifluoromethyl);

10 R<sup>21</sup> is selected from the group consisting of hydrogen, alkyl, aryl, aralkyl, alkylcarbonyl, arylcarbonyl and aralkylcarbonyl; wherein the aryl portion is optionally substituted with one or more substituents independently selected from halogen, alkyl, alkoxy, halogenated alkyl or nitro;

15 p is an integer selected from 0 to 3;

q is an integer selected from 0 to 3;

20 R<sup>22</sup> and R<sup>23</sup> are each independently selected from the group consisting of halogen, alkyl, alkoxy, amino, alkylamino, dialkylamino, nitro, cyano, carboxy, alkoxycarbonyl, aryloxy, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

or a pharmaceutically acceptable salt thereof.

41. The compound as in Claim 40 wherein

25 R<sup>A</sup> is selected from the group consisting of hydrogen, alkyl, aryl and aralkyl; wherein the aryl portion of any of the groups is optionally substituted with one to three substituents independently selected from halogen, lower alkyl, lower alkoxy, halogenated lower alkyl, amino, lower alkylamino, di(lower alkyl)amino, arylamino, aralkylamino, azo, nitro, cyano, aryl, aralkyl, aryloxy, carboxy, lower alkoxycarbonyl, 30 aryloxy, carbonyl, lower alkylthio and arylthio;

R<sup>B</sup> is selected from the group consisting of hydrogen, alkyl, halogenated lower alkyl, amino, lower alkylamino, di(lower alkyl)amino, amino-lower alkyl, lower alkyl-amino-lower alkyl, di(lower alkyl)amino-lower alkyl, aryl, aralkyl, cycloalkyl,



cycloalkyl-lower alkyl, heteroaryl, heteroaryl-lower alkyl, lower alkoxy-lower alkyl, aryloxy, aryloxy-lower alkyl, lower alkoxycarbonyl-lower alkyl and dehydroabietyl; wherein the aryl, cyloalkyl, heteroaryl or heterocycloalkyl portion of any of the groups is optionally substituted with one to three substituents independently selected from

5 halogen, lower alkyl, lower alkoxy, halogenated lower alkyl, amino, lower alkylamino, di(lower alkyl)amino, arylamino, aralkylamino, azo, nitro, cyano, aryl, aralkyl, aryloxy, carboxy, lower alkoxycarbonyl, aryloxycarbonyl, lower alkylthio and arylthio;

alternatively,  $R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form a ring structure selected from the group consisting of heteroaryl and  
10 heterocycloalkyl; wherein the heteroaryl or heterocycloalkyl group is optionally substituted with one to two substituents independently selected from halogen, lower alkyl, lower alkoxy, lower alkoxycarbonyl, trifluoromethyl, lower alkylcarbonyl, amino, lower alkylamino, di(lower alkyl)amino, arylamino, azo, nitro or cyano.

15  $R^C$  is selected from the group consisting of lower alkyl, aralkyl, lower alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, ( $\pm$ )-N-benzoyl-amino-lower alkylcarbonyl and [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-lower alkylcarbonyl;

20  $R^D$  is selected from the group consisting of alkyl, aryl, aralkyl, ( $\pm$ )-N-benzoyl-amino-lower alkyl, [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-lower alkyl and biphenyl; wherein the alkyl or aryl portion of the aryl or aralkyl group is optionally substituted with one to two substituents independently selected from  
25 halogen, lower alkyl, lower alkoxy, amino, lower alkylamino, di(lower alkyl)amino, azo, nitro, cyano or trifluoromethyl);

$R^{21}$  is selected from the group consisting of hydrogen, lower alkyl, aryl, aralkyl, lower alkylcarbonyl, arylcarbonyl and aralkylcarbonyl (wherein the aryl portion of the aryl, aralkyl, arylcarbonyl or aralkylcarbonyl group is optionally substituted with one to  
30 two substituents independently selected from halogen, lower alkyl, lower alkoxy or trifluoromethyl);

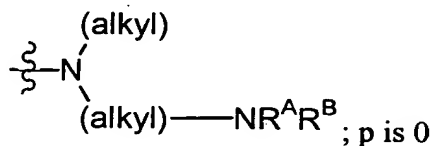
p is an integer from 0 to 2;

q is an integer form 0 to 2;

R<sup>22</sup> and R<sup>23</sup> are each independently selected from the group consisting of halogen, lower alkyl, lower alkoxy, amino, lower alkylamino, di(lower alkyl)amino, nitro, cyano, carboxy, lower alkoxycarbonyl, phenyloxycarbonyl, aminocarbonyl, lower alkylaminocarbonyl and di(lower alkyl)aminocarbonyl;

5 or a pharmaceutically acceptable salt thereof.

42. The compound as in Claim 41 wherein R<sup>20</sup> is



and q is 0.

10 43. The compound as in Claim 42 wherein

R<sup>A</sup> is selected from the group consisting of hydrogen, lower alkyl and aralkyl;

R<sup>B</sup> is selected from the group consisting of hydrogen, lower alkyl, halogenated lower alkyl, aralkyl, substituted aralkyl (wherein the substituents on the aralkyl are one to three independently selected from halogen, lower alkyl, lower alkoxy or trifluoromethyl), alkoxyalkyl, cycloalkyl-alkyl, dehydroabietyl, di(lower alkyl)-amino-lower alkyl, biphenyl, heteroaryl, substituted heteroaryl (wherein the substituents on the heteroaryl group are one to two independently selected from halogen or lower alkyl), heteroaryl-lower alkyl, aryloxy-lower alkyl and lower alkoxycarbonyl-lower alkyl; and

R<sup>21</sup> is hydrogen;

20 or a pharmaceutically acceptable salt thereof.

44. The compound as in Claim 43, wherein

R<sup>A</sup> is selected from the group consisting of hydrogen, methyl, ethyl and benzyl; and

25 R<sup>B</sup> is selected from the group consisting of hydrogen, methyl, propyl, n-butyl, benzyl, phenylethyl, methoxypropyl, cyclohexylmethyl, 3-chlorobenzyl, 2,4-dimethoxybenzyl, 2-ethoxybenzyl, 2,5-difluorobenzyl, dehydroabietyl, 3,4-dimethoxybenzyl, diethylaminopropyl, 4-bromo-2-pyridyl, dimethylaminoethyl, 4-biphenyl, 2-furanylmethyl, 3-iodobenzyl, 2,2,2-trifluoroethyl, 3,4-difluorobenzyl, 2-theinylethyl, 3,5-dimethyl-2-pyridyl, 2-(ethoxy)acetyl, 2-methoxybenzyl, 4-bromobenzyl, 3,5-ditrifluoromethylbenzyl, 3-methoxyphenylethyl, 3,4,5-

trimethoxybenzyl, 4-methoxyphenylethyl, 4-imidazolylethyl, 2-trifluoromethylbenzyl, 3-methoxybenzyl, 3-methylbenzyl, 3,5-dimethoxybenzyl, 2-bromobenzyl, 4-fluorobenzyl, 1-naphthylmethyl, phenoxyethyl, 4-trifluoromethylbenzyl, 3-pyridyl, 2-methylbenzyl, 2-fluorobenzyl and 3,4-dimethoxyphenylethyl;

5 or a pharmaceutically acceptable salt thereof.

45. The compound as in Claim 44 wherein

$R^A$  is selected from the hydrogen, methyl and benzyl; and

10  $R^B$  is selected from the group consisting of methyl, methoxypropyl, cyclohexylmethyl, 3-chlorobenzyl, 2,5-difluorobenzyl, phenylethyl, 4-bromo-2-pyridyl, dimethylaminoethyl, n-butyl, 2-furanylmethyl, 3,4-difluorobenzyl, 2-thienylethyl, 4-bromobenzyl, 3-methoxyphenylethyl, 3,4,5-trimethoxybenzyl, benzyl, 3-methylbenzyl and phenoxyethyl;

or a pharmaceutically acceptable salt thereof.

15

46. The compound as in Claim 45 wherein

$R^A$  is selected from the group consisting of hydrogen and methyl; and

20  $R^B$  is selected from the group consisting of methyl, methoxypropyl, 2,5-difluorobenzyl, 3,4-difluorobenzyl, 4-bromobenzyl, 3,4,5-trimethoxybenzyl, benzyl, 3-methylbenzyl and n-butyl;

or a pharmaceutically acceptable salt thereof.

47. The compound as in Claim 46 wherein  $R^A$  is methyl and  $R^B$  is methyl; or a pharmaceutically acceptable salt thereof.

25

48. The compound as in Claim 42, wherein

$R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form a ring structure selected from the group consisting of heteroaryl, heterocycloalkyl and tertiarybutoxycarbonyl substituted heterocycloalkyl; and

30

$R^{21}$  is hydrogen;

or a pharmaceutically acceptable salt thereof.

49. The compound as in Claim 48, wherein

$R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form a ring structure selected from the group consisting of N-pyrrolidinyl, N-morpholinyl, N-imidazolyl, N-1,2,3,4-tetrahydroisoquinlinyl, N-hexamethylenimine and N-(4-tertiarybutoxycarbonyl)piperazinyl;

5 or a pharmaceutically acceptable salt thereof.

50. The compound as in Claim 49 wherein

$R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form a ring structure selected from the group consisting of N-morpholinyl and N-(4-tertiarybutoxycarbonyl)piperazinyl;

10 or a pharmaceutically acceptable salt thereof.

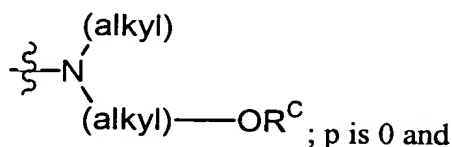
51. The compound as in Claim 50 wherein

$R^A$  and  $R^B$  are taken together with the nitrogen atom to which they are bound to form N-morpholinyl; or a pharmaceutically acceptable salt thereof.

15

52. The compound as in Claim 41 wherein  $R^{20}$  is

20



53. The compound as in Claim 52 wherein

$R^C$  is selected from the group consisting of arylcarbonyl, ( $\pm$ )-N-benzoyl-2-aminoalkylcarbonyl and [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-alkylcarbonyl; and

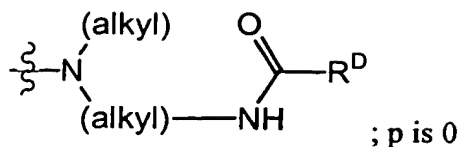
$R^{21}$  is hydrogen;

25 or a pharmaceutically acceptable salt thereof.

54. The compound as in Claim 53, wherein

$R^C$  is selected from the group consisting of benzoyl, ( $\pm$ )-N-benzoyl-2-aminopropionoyl and [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-4-pentanoyl; or a pharmaceutically acceptable salt thereof.

30



55. The compound as in Claim 41 wherein  $\text{R}^{20}$  is and q is 0.

56. The compound as in Claim 55 wherein

5  $\text{R}^{\text{D}}$  is selected from the group consisting of ( $\pm$ )-N-benzoyl-2-aminoalkyl, [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-alkyl, alkyl, substituted aryl (wherein the substituents on the aryl are independently selected from azo, nitro, halogen, alkoxy, trifluoromethyl), biphenyl, aralkyl and substituted aralkyl (wherein the alkyl portion of the aralkyl group is substituted with a substituent selected from  
10 halogen); and

$\text{R}^{21}$  is selected from the group consisting of hydrogen, alkylcarbonyl and substituted arylcarbonyl (wherein the substituent on the aryl portion of the arylcarbonyl group is selected from halogen or trifluoromethyl);  
or a pharmaceutically acceptable salt thereof.

57. The compound as in Claim 56 wherein

$\text{R}^{\text{D}}$  is selected from the group consisting of ( $\pm$ )-N-benzoyl-2-aminoeth-2-yl, [3aS-(3 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )]-hexahydro-2-oxo-1H-thieno[3,4-d]imidazole-but-4-yl, 1-chloro-1-phenyl-methyl, 3-azo-6-nitrophenyl, pentacecanyl, 4-biphenyl, 4-butoxyphenyl, 4-  
20 trifluoromethylphenyl, 3-fluorophenyl and propyl; and

$\text{R}^{21}$  is selected from the group consisting of hydrogen, propylcabronyl, 3-fluorophenylcarbonyl and 4-trifluoromethylphenylcarbonyl;  
or a pharmaceutically acceptable salt thereof.

25 58. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 40.

59. A pharmaceutical composition made by mixing a compound of Claim 40 and a pharmaceutically acceptable carrier.

60. A process for making a pharmaceutical composition comprising mixing a compound of Claim 40 and a pharmaceutically acceptable carrier.

61. A method of reducing ischemic death in a cell population comprising contacting at least a portion of the cell population with a prophylactically effective amount of the compound contained in the pharmaceutical composition of claim 40.

62. The method of claim 61, wherein at least one cell in the cell population is selected from the group consisting of a neuronal cell, a glial cell, a cardiac cell, a lymphocyte, a macrophage and a fibroblast.

63. A method of reducing death in a cell population comprising neuronal cells in response to a traumatic event comprising contacting the neuronal cells with a prophylactically effective amount of the compound as in Claim 40 prior to, during, or following the traumatic event.

64. A method of reducing neuronal cell death in response to a traumatic event in a subject, comprising administering to the subject a prophylactically effective amount of a compound as in Claim 40 prior to, during, or following the traumatic event.

65. The method of claim 64, wherein the traumatic event is selected from the group consisting of a medical disorder, a physical trauma, a chemical trauma and a biological trauma.

66. The use of a compound as in Claim 40 for the preparation of a medicament for reducing the likelihood of a cell's undergoing ischemic death, in a subject in need thereof.